

REMARKS

This paper is in response to the non-final Office Action dated June 25, 2004. Applicants respectfully assert that this Reply is fully responsive to each of the objections raised in the outstanding Office Action.

Claims 1-12 and 14-16 were pending in the application. Claims 4, 9, 11, 13 and 16 have been canceled without prejudice to Applicants' right to pursue the canceled subject matter in other applications. Applicants respectfully request the withdrawal of any objections or rejections of the canceled claims.

Claims 1-3, 5-6, 8, 10, 12 and 15 have been amended and new Claim 17 added. The amended and new claims are fully supported by the originally filed claims and the specification. Claim 17, which is dependent on claim 12, finds support in the originally filed specification at, for example, page 23, line 1. As such, no new matter has been added and claims 1-3, 5-8, 10, 12, 14-15 and 17 are pending.

The Office Action notes that "applicant has not filed a certified copy of the 99/09990 application as required by 35 U.S.C. 119(b). The instant application is a 371 of ✓
✓PCT/FR00/02130 and the International Bureau received the priority document on October 17, 2000 (see enclosed copy of Form PCT/IB/304) . Thus, Applicants respectfully submit that, in accordance with Rule 17.25 PCT, a certified copy of the priority document is not required to be separately provided.

The disclosure and claims are objected to because of informalities. Applicants have corrected such informalities by amendments herein to the specification. No new matter has

been added by these amendments. In particular, the specification (see, e.g., page 7) demonstrates that “the expected phenotype” is the phenotype that is linked to the presence of the transgene, and the specification has been amended accordingly. Claim 16, which is objected to under 37 CFR 1.75(c), has been canceled. Accordingly, Applicants believe that these objections have been obviated.

THE CLAIMS ARE ENABLED

Claims 1-12 and 14-16 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the enablement requirement because the claims allegedly “contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.” Office Action at page 3.

Applicants respectfully disagree with these rejections, and submit that the pending claims, as amended, are fully enabled by the originally filed specification, drawings and claims. As a preliminary matter, Applicants respectfully request the withdrawal of rejections of the canceled Claims 4, 9, 11, 13 and 16.

The instant Office Action appears to state that the presently claimed invention is not enabled because (1) it refers to “a line suited to transformation” but only describes A188 (Office Action at page 4); (2) it refers to “selection of transformants that contain the T-DNA, in the genome of the line of interest” but only describes RFLP (Office Action at page 4); (3) it refers to “selection of transformants that contain the T-DNA, in the genome of the line of interest” but just mentions two different techniques per *Southern and Sambrook* to perform said selection (Office Action at pages 4-5) (cf. (2) above); (4) it refers to a “line of interest [that] is

not described” (Office Action at page 5); (5) it refers to a “second line of interest” that is not described (Office Action at page 5); (6) it is broadly claimed to be applicable to different plant types (Office Action at page 5-6); (7) it refers to any protein conferring agronomical properties or resistance to disease, which protein is not described (Office Action at page 6); (8) it refers to a commercial line that is not described (Office Action at page 6); (9) it refers to different plants but only describes maize (Office Action at page 6); and (10) it refers to, but does not describe, a plant free of linked fragments which “may be the subject of a genetic burden” (Office Action at page 6).

Pointing to the disclosures of two references cited in the instant specification at pages 6-7, the Office Action also claims unpredictability in the art regarding methods of making isotransgenic lines, and further takes issue with (11) the number of markers necessary to follow-up on the selection (Office Action at pages 7-8); and (12) alleges unpredictability of recovering pertinent molecular markers (Office Action at page 8). Also, the instant specification’s disclosure based on Ishida et al., Zeven et al., and Young et al. are asserted to evidence difficulty in breaking linkage drag. Applicants note that the Examiner’s arguments for lack of enablement appear to be at odds with, and indeed are undercut by, the Examiner’s later assertions that the individual steps of the presently claimed methods were fully known in prior art references such that it would have been obvious to one of skill in the art to combine the several cited references to reach the claimed invention. *See* Office Action at pages 17-18.

Although the prior art, in fact, has evidenced difficulty in obtaining true isotransgenic lines, this is precisely the problem solved by the present invention. As recognized in the Examiner, the linkage drag might not be broken if the transgene is inserted within the non-

agronomic parent. Office Action at page 7. However, step (b) of pending Claim 1 squarely addresses this problem in making it possible to avoid linkage drag by pre-selecting the plants that will be regenerated and used in the backcross scheme.

The Examiner's reference to the instant specification at page 24, lines 15-19, is misplaced in that this section of the specification actually refers to the problem of the prior art (i.e., wherein A188 is transformed). Applicants respectfully direct the Examiner's attention to specification at page 24, lines 20-25, wherein the advantages of the presently claimed method are indicated.

Furthermore, although the Office Action states that "it is more likely that the transgene would be inserted into the genomic region derived from the non-agronomic transformable parent," and also states that "hotspots" exist -- contrary to the teachings of the specification (page 6, lines 5-10) -- no evidentiary basis is proffered, in contravention of MPEP 2164.04, for these conclusory statements.

Applicants first address each of the above-listed points in turn:

(1) The instant specification refers to the A188 maize line as the "suited for transformation." Indeed, a person of ordinary skill in the art can make and use the invention using the A188 line thus enabling the presently claimed invention. Furthermore, since the invention does not relate to identifying lines suited for transformation, but instead to using such lines, a person of ordinary skill in the art would choose a line suitable for transformation to make and use the claimed methods.

The instant specification also teaches that lines other than A188 can be used for transformation. For example, certain lines (e.g., HiII) are described as suitable with the

appropriate protocol in WO 98/32326, which is cited at page 22 of the instant specification. This demonstrates that, in the case of maize, other lines are known in the art.

(2) and (3) Methods for analyzing and comparing genomes of transformed plants are known in the art. Indeed, the Office Action cites art that demonstrates this (e.g., Does et al.; Welsh et al.). RFLP is described in the specification by reference to a publication and is also exemplified. Although other suitable methods known in the art may be used in accordance with the invention, explicit description of the method using RFLP enables the person of ordinary skill in the art to make and use the presently claimed invention.

To adapt the exemplified techniques for a specific type of plant or genome is only routine work, as the level of skill in this art is relatively high. As indicated in Zeven et al., as early as 1983 (i.e., more than 15 years before the instant application's filing date) it was already possible to follow-up linkage drag (which requires greater precision than simply analyzing a chromosome because linkage drag relates to small parts of chromosomes of one line introgressed in another line). The law on enablement does not preclude all experimentation necessary to make and use the invention, only undue experimentation. *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988) (“[T]he claimed invention [is] enabled so that any person skilled in the art can make and use the invention without undue experimentation.” The experimentation to perform such routine adaptation of the exemplified techniques is not nearly “undue.”

Indeed, other suitable methods for analyzing a genome to identify the insertion of the T-DNA carrying the transgene merely can be considered merely members of a genus of known diagnostic methods (of which RFLP is but an example). Other known methods include

sequencing the T-DNA borders, mapping techniques, Southern blotting, etc. Applicants respectfully submit that the whole genus of diagnostic methods is enabled, in accordance with MPEP 2164.02 which states that: "Proof of enablement will be required for other members of the claimed genus only where adequate reasons are advanced by the examiner to establish that a person skilled in the art could not use the genus as a whole without undue experimentation." The Examiner has not advanced adequate reasons as to why the person of ordinary skill in the art would require undue experimentation to identify the localization of the transgene, where such work is routine in the art when performing transformation of plants (see, e.g. Ishida et al., which was cited by the Examiner). Since the techniques cited in the specification are well known by the person skilled in the art and can be applied without undue experimentation, the claim scope encompassing such known techniques are enabled even though some adaptation or optimization experiments may be necessary. *See also United States v. Telectronics, Inc.*, 857 F.2d 778, 8 USPQ2d 1217 (Fed. Cir. 1988), cert. denied, 490 U.S. 1046 (1989).

(4) and (5) The present invention is directed to the production of a transgenic line that is isogenic to a line of interest. Thus, any line that the person of ordinary skill in the art finds of interest would be in accordance with the claimed methods. Further, note that the specification provides examples of lines (elite lines) that can be considered as "lines of interest" (see, e.g., specification at page 2, lines 4-14). This nomenclature is well known in the art and therefore the person of ordinary skill in the art would immediately understand what is meant by this term, and understand how to use such plant lines in the context of the invention.

(6) The Office Action states that the specification "very broadly claims 'a crop plant, vegetable plant, and a floral plant' (see, Claim 6). These terms are very broad and are not

defined in the specification and therefore would not allow one who is skilled in the art the ability to use the claimed invention.” Office Action at pages 5-6. Claim 6 has been amended to recite “crop plants, vegetables, and flowers.” As such, Applicants respectfully assert that one of ordinary skill in the art, even without resorting to a dictionary to find their ordinary meaning, would fully appreciate what is meant by these claim terms and would be able to use the claimed invention.

(7) The Office Action states that “the specification does not fully disclose a protein which confers agronomic properties and/or properties of resistance to disease.” Office Action at page 6. Applicants respectfully direct the Examiner’s attention to the instant specification at pages 11-14, in which examples of proteins that confer agronomic properties and/or properties of resistance to disease are well described.

(8) Claim 8 has been amended to recite that the line of interest is a commercial elite line. At least one document (i.e., Armstrong et al.) cited by the Examiner teaches such a commercial line (873). Furthermore, commercial lines were widely known to, and used by, persons of ordinary skill in the art.

(9), (10), (11) and (12) The invention is **generic** and the individual steps of the claimed methods are known in the art, and thus enabled for any plant. The genus is the plants, and maize is an exemplified member of this genus. A person of ordinary skill in the art could perform the presently claimed invention on a plant species, including maize, from his/her general knowledge of the art by selecting plant lines that are well suited to transformation and plant lines “of interest” according to the invention. MPEP 2164.02 indicates that “Proof of enablement will be required for other members of the claimed genus only where adequate reasons are advanced

by the examiner to establish that a person skilled in the art could not use the genus as a whole without undue experimentation.” Applicants respectfully submit that the reasoning in the Office Action fall far short of explaining why a person of ordinary skill in the art, using the teachings of the instant specification, would have not been able to prepare hybrids, select the desired transformants, and perform the backcrosses (e.g., by identifying the genetic origin of a chromosome and following backcrosses using markers -- none technically challenging) for other plant species.

Furthermore, reliance on a document published approximately a decade before the present applicant’s filing date (i.e., Welsh et al., 1990) to argue lack of enablement improperly ignores the knowledge in the art at the date of filing. Moreover, Welsh et al. (at page 7216, column 2, 5th paragraph) actually teach that “AP-PCR will work with most genome and species,” having successfully tested it on rice, maize and human genomes. Notably, Welsh et al. further teach that this method does not require any prior sequence information (abstract). Thus, Welsh et al. actually demonstrate that it is within the purview of the skilled artisan to discriminate genomes.

Staub et al. compare different marker systems. The passage cited in the Office Action is taken out of context and actually supports the view already developed above that a person of ordinary skill in the art can choose an appropriate marker system in accordance with the presently claimed invention. Staub et al. (page 731, column 3, 1st paragraph) clearly disclose marker systems, such as RFLP, SSR, AFLP, and thereby provide teachings related to choosing appropriate marker systems.

With regard to Claims 12 and 17, which do not claim a specific line, Applicants respectfully submit that the deposit requirements are not applicable. In the present case, claims 12 and 17 are no different than claims directed to a transgenic plant in, for example, a patent relating to a gene useful for transformation. Here, the claimed plant lines are well defined and the methods according to pending Claim 1 enables the person of ordinary skill in the art to make them.

The Enablement Standard

MPEP 2164.01 states: “Any analysis of whether a particular claim is supported by the disclosure in an application requires a determination of whether that disclosure, when filed, contained sufficient information regarding the subject matter of the claims as to enable one skilled in the pertinent art to make and use the claimed invention.”

Thus, enablement is demonstrated if one of ordinary skill in the art can perform the invention using the teachings of the instant specification and those of the prior art. Applicants respectfully assert that a proper understanding of the prior art and of the present invention as a whole firmly supports the conclusion that the claims are enabled.

The present invention relates to a **generic** method useful for obtaining isotransgenic lines which, as defined in the specification, differ from the line of interest by the presence of the transgene and T-DNA. In direct contrast, transformation methods of the prior art do not lead to isotransgenic lines as defined in the invention. See, e.g., Ragot et al.

In the first step (a) of the presently claimed method, a hybrid plant is obtained by crossing a parental line suited for transformation with another line of interest, which may be an elite line (see, e.g., page 2 of the instant specification). Cells of the hybrid plant are then, by e.g.

the *Agrobacterium* technique, transformed with a vector carrying a T-DNA containing a transgene to obtain an isotransgenic line. The line of interest is then compared to the isotransgenic line so obtained.

Transformation methods are well known in the prior art. See, e.g., Ishida et al. (transformation of maize) and Hiei et al, (transformation of rice). By the date of the presently claimed method, virtually all plants could be transformed with *Agrobacterium*, and this was well known in the art. Notably, transformation was generally performed using specific lines - also well known in the prior art - that are more suited than others for *Agrobacterium*-mediated transformation (with respect to, *inter alia*, infection, gene transfer or regeneration potential). As such, transformation techniques required in step (a) were well within the purview of one of ordinary skill in the art.

Accordingly, in the context of the present invention, one of ordinary skill in the art - guided by the teachings of the instant specification - would have been able to perform the required transformation methods, indeed irrespective the nature of the transgene. In particular, any transgene that can confer upon it resistance to diseases/pathogens and/or an improved agronomic or nutritional quality (amino acids, oil, starch, etc.) can be used in accordance with the present invention (see, e.g., page 7 of the instant specification). Additionally, many suitable transgenes are provided on pages 11-14 of the instant specification. Moreover, the transformed cells can be selected using a reporter or selection gene (see, e.g., page 14 of the instant specification). One of ordinary skill in the art would recognize that the basic techniques underlying the principles set forth in the instant specification were well known in the art.

The second step (b) of the method requires performing an analysis of the transformed cells so as to select only those cells where T -DNA has integrated within the genome of the line of interest. This second step is important because such a selection identifies isotransgenic lines where no part of the genome of the line used for transformation is present. This analysis is performed by any suitable method known in the art, as described in the specification. Tools were widely available, first, to determine the number and location of T-DNA insertions (see, e.g., Does et al.), and second, to discriminate between two plant genomes (see, e.g., Ragot et al.; Young et al. (measuring introgression of part of a chromosome of one line within another line); Welsh and McClelland, (which clearly state that their method can distinguish strains and lines within a species)). Accordingly, one of ordinary skill in the art - guided by the teachings of the instant specification - would have been able to perform the selection analysis using routine diagnostic methods known and available in the prior art.

The third and fourth steps (c) and (d), respectively, require performing backcrosses, which again is a technique well known in the art (see, e.g., Ragot et al.). The claimed invention calls for backcrosses between with the transformed line selected in step (c) and the line of interest in order to completely remove chromosomal material from the transformed line. As such, the presently claimed method defines steps for quickly obtaining isotransgenic lines where no fragment of a transformation line is present near the transgene.

Most importantly, as explained above, the basic techniques required in each and every step of the claimed methods were well known in the prior art and, therefore, were available to the person of ordinary skill in the art as of the earliest priority date of the instant application. Accordingly, such skilled artisans would reasonably have been able to perform the claimed

methods, without undue experimentation, by taking into account the nature of the transgene to be employed, nature of the line suited to transformation, nature of the line of interest, markers for performing the genome analysis, and the necessary backcrosses.

In sum, the claimed methods for producing isotransgenic lines require transforming a suitable line, selecting appropriate transformants, and performing backcrosses with a line of interest. The performance of each of these method steps are known from the prior art (see, e.g., Ragot et al.), which evidences that the required materials (i.e., the line suitable for transformation and the line of interest), as well as the associated methods, were well known in the art. Accordingly, from the teachings of the instant specification and that in the prior art, the person of ordinary skill in the art would have been enabled to make and/or use the invention as of the earliest priority date of the instant application. As such, Applicants respectfully request that the rejections for lack of enablement under 35 U.S.C. § 112, first paragraph, be withdrawn.

THE CLAIMS ARE SUPPORTED BY THE SPECIFICATION

Claims 1-12 and 14-16 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. Office Action at pages 10-12. Applicants respectfully disagree.

35 U.S.C. § 112, first paragraph indicates that the “specification shall contain a written description of the invention” (emphasis added). As indicated above, the present invention is directed to obtaining isotransgenic lines by combining multiple steps (transforming a hybrid, specifically selecting primary transformants, and backcrossing), each step being known in the art. The invention is described as soon as the steps of the method are well enunciated. This is both necessary and sufficient to describe the invention.

“Compliance with the written description requirement is essentially a fact-based inquiry that will necessarily vary depending on the nature of the invention claimed.” *Enzo Biochem. v. Gen-Probe*, 63 USPQ2d 1609 (Fed. Cir. 2002). Furthermore, “The PTO has the initial burden of presenting evidence or reasons why persons skilled in the art would not recognize in the disclosure a description of the invention defined by the claims.” In the present case, the nature of the claimed invention is a combination of known methods. Listing these methods and how to combine them ensures compliance with the written description requirement. The Office Action fails to indicate why a person of ordinary skill in the art would not have recognized in the disclosure a description of the presently claimed invention.

Indeed, the documents cited in the Office Action demonstrate that the methods of transforming hybrids, analyzing transformants, and performing backcrosses were known in the prior art (see, e.g., Ishida et al.; Ragot et al.). Analysis of transformants and strategy for backcrosses make use of molecular marker techniques, which are easily adaptable for use in species in addition to maize. In particular, Hiei et al. (cited by the Examiner) demonstrates the analysis of boundaries of T-DNA in rice (which is one step performed when selecting the transformants). Other documents are already of record which prove that a person of ordinary skill in the art had a broad knowledge of these methods.

In summary, the invention as claimed (i.e., a generic combination of known methods in the art) is thus clearly described. This ensures that Applicants were in possession of the invention at the time of filing, and that Applicants have disclosed in the instant specification sufficient information to place the public in possession of the invention. All the steps necessary

for performing the invention have been disclosed, and the public can thus reproduce the invention.

Applicants note that, in asserting that the specification does not comply with the written description requirement, the Office Action relies on the MPEP and *University of California v. Eli Lilly*, 119 F.3d. 1559 (Fed. Cir. 1997), *cert. denied* 523 U.S. 1089 (1998). The cited portions of the MPEP and *Eli Lilly*, which relate to situations where a gene is claimed without its sequence (structure), are not applicable to the present case. The presently claimed method does not claim specific lines or markers, but makes use of such lines and marker in a combination of methods known in the art. As discussed above, the person of ordinary skill in the art can identify lines to use for generating the hybrid, techniques to perform the transformation, markers to analyze the transformants, and techniques to perform the backcrosses. Thus, the generic method in accordance with the present invention is applicable for suitable plant species. As indicated in *Eli Lilly*, there is no description of a named material “in the absence of knowledge as to what that material consists.” In the present case, and as indicated above, the person of ordinary skill in the art would appreciate and be able to select a line suitable for transformation and a line of interest, and would be knowledge with respect to the number of backcrosses required to perform the claimed methods.

Accordingly, Applicants respectfully request that the rejections based on insufficient written description under 35 U.S.C. § 112, first paragraph, be withdrawn.

THE CLAIMS ARE DEFINITE

Claims 1-9, 11-12 and 14-16 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite due to use of the phrase “each backcross until” in independent claim 1. Office Action at pages 12-13. Although Applicants assert that one of ordinary skill in the art would fully understand this phrase as used in the claims, Claim 1 has been amended to more particularly point out and distinctly claim what Applicants consider to be their invention.

Claims 9 and 16, which are also rejected under 35 U.S.C. § 112, second paragraph (Office Action at page 13), have been canceled thus obviating the rejections of these claims. As such, Applicants respectfully request that the rejections under 35 U.S.C. § 112, second paragraph, be withdrawn.

THE CLAIMS ARE NOT ANTICIPATED BY RAGOT

Claims 11-12 and 16 are rejected under 35 U.S.C. § 102(b) as allegedly being unpatentable over Ragot et al., 1994 (hereinafter “Ragot”). Applicants respectfully request withdrawal of the rejections of Claims 11 and 16 which have been canceled without prejudice.

The Office Action alleges that Ragot “teach the introgression of a transgene construct from a transformed corn plant into an elite inbred corn line via backcrossing to the elite inbred line.” Office Action at page 14. The Office Action also alleges that “[t]he isotransgenic corn plants taught by Ragot et al. differ from the claimed corn plants only in their method of making.” Office Action at page 14. Applicants respectfully disagree.

As indicated in the specification and above, the invention makes it possible to stably integrate a transgene within the genome of a line of interest. Indeed, the invention is not

merely transformation of hybrid plant, selection of plants containing the transgene and backcrossing within the desirable line following selection. The transformed plants must have integrated the transgene in the genome of the parental line of interest. This ensures that no recombination events are needed for introgression of the transgene when performing the backcrosses.

Thus, no remaining DNA originating from the line suited for transformation will ultimately be found in the isotransgenic line, which only contains the T-DNA containing the transgene. With this in mind, it is apparent that the claimed lines of the invention differ from Ragot in several respects. Ragot clearly mentions the production of “near isogenic lines” (page 45, introduction). Indeed, Ragot introgresses a transgene from a Lancaster maize line within a Stiff Stalk line (page 46, plant material). These are two different lines. Figure 1-d clearly demonstrates that the transgene locus remains heterozygous after four backcrosses (chromosome 1), while all other chromosomes have been homozygous since the third backcross (see also Figure 1-c). Actually, Figures 1-c and 1-d indicate that the limiting step is obtaining the appropriate recombination events around the transgene locus. Page 54 (line 1) indicates that 0.64 % of the genome remains genome of the parent (Lancaster) line. Since some Lancaster genomic sequences nevertheless remain, it follows that Ragot does not describe any isotransgenic line as compared to a line of interest (i.e., Stiff Stalk), wherein said isotransgenic line only differs from said line of interest by the presence of the T-DNA containing the transgene. In fact, Ragot acknowledges the presence of a linkage drag and discusses this point. *A contrario*, when performing the method of the invention, the linkage drag around the transgene would be perfectly null, as the transgene would already be in the genome of the line of interest before the backcrosses (due to the selection step b of the presently claimed method).

Accordingly, Applicants submit that the isotransgenic lines of Claim 12 and new Claim 17 are clearly distinct from those lines disclosed in Ragot. Moreover, the respective lines differ not only by the method of making but also by their structure (lack of linkage drag). As such, Ragot cannot anticipate the claimed invention, and Applicants respectfully request that the rejections under 35 U.S.C. § 102(b) in view of Ragot be withdrawn.

THE CLAIMS ARE NOT OBVIOUS IN VIEW OF THE CITED ART

Claims 1-12 and 14-16 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Ishida et al., 1996, Nature Biotech. 14:745-750 (“Ishida”) in view of Does et al., 1991, Plant Mol. Biol. 17:151-153 (“Does”), Hiei et al., 1994, Plant Journal 6:271-282 (“Hiei”), Armstrong et al., 1992, Theoretical and Applied Genetics 84:755-762 (“Armstrong”) and Ragot.

The Office Action alleges that “it would have been obvious to one of ordinary skill in the art at the time the invention was made [] to have used the method of Ishida et al. to transform hybrid plants and to modify that method by incorporating that of Does et al. and Hiei to assay the T-DNA integrated into the genome of said plants and furthermore, to use the backcrossing and RFLP method of Armstrong et al. to develop isotransgenic plants containing a desired transgene; given the desirability of isogenic transgenic lines and success in obtaining them as taught by Ragot et al.” Office Action at page 17. Applicants respectfully disagree.

“To establish prima facie obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art.” MPEP 2143.03. In the present invention, an important step of the claimed method is to select only hybrid primary transformants in which the T-DNA has integrated only into the genome of the parental line of interest.

As indicated by the Examiner, this step is not taught by Ishida (Office Action at page 16). Does teaches a method to estimate the number of T-DNA copies in transgenic plants using inverse PCR, but fails to teach or suggest backcrossing the obtained transgenic plants or transformed hybrids.

Armstrong fails to teach transformation but relates only to the regenerative ability of the inbred line B73 in which parts of the A188 genome have been introgressed. At no point were the different BC populations transformed. Thus, Armstrong is silent on selecting hybrid primary transformants. Furthermore, since Armstrong does not teach transformation it necessarily does not teach producing isotransgenic lines by this method. The only pertinent teaching offered by Armstrong is an ability to finely analyze backcrosses using RFLP markers.

None of the cited documents teaches or suggests that a selection of hybrid primary transformants, in which the T-DNA has integrated only into the genome of the parental line of interest, must be performed after transformation and before starting the backcrosses. Indeed, when taken in combination, one of ordinary skill in the art would have used the method of Ishida (transformation of hybrid plant), the teachings of Does and Hiei (analysis of the site and number of integration loci of the T-DNA), and the RFLP-assisted backcrossing methods of Armstrong to follow-up the introgression of the transgene in a line of interest as per Ragot (Ragot at page 45 - teaching that marker-assisted backcrosses accelerate the possibility to obtain near isotransgenic lines). Due to the genetic drag, it would not have been possible to obtain true isotransgenic lines (*see also* Zeven et al. and Young et al.). As such, even in combination, the cited references do not reach the claimed invention, at least by the omission of the claimed method step **(b)** requiring the selection of specific transformants.

Moreover, the claimed invention demonstrates unexpectedly superior results by (1) reducing the number of necessary backcrosses since the first backcross is performed on a material that already contains 50 % of the genome of the line of interest with which the backcrosses are performed (due to the fact that hybrids are transformed in step (a)); and (2) simplifying the follow-up of the backcrosses since there is no need to follow-up recombination events around the transgene when introgressing it within the genome of the line of interest (as a result of selection step (b)). This will also ease the backcrossing scheme to obtain true isotransgenic lines when compared to the line of interest because the selection step (b) ensures that the transgene will be within the genome of said line of interest.

Moreover, Applicants respectfully assert that by finding bits and pieces of the claimed invention in the prior art and piecing them together in attempt to meet the claimed invention, the Examiner has used Applicants' own disclosure as a blueprint to assemble the cited art. Applicants note that not one of the cited references contains in its disclosure the motivation to combine its teachings with any of the other cited art. None of the cited references refer to any other of the cited art and no such suggestion to combine can reasonably be found within the cited references. This exercise then appears to constitute nothing more than hindsight reconstruction of the claimed invention. Accordingly, Applicants respectfully submit that neither Ishida, Hiei, Does, Armstrong, nor Ragot provide any motivation to combine their respective teachings, and neither singly nor taken together, teach or suggest the presently claimed invention.

As such, Applicants respectfully request that the rejections under 35 U.S.C. § 103(a) in view of the combination of Ishida, Hiei, Does, Armstrong, and Ragot be withdrawn.

CONCLUSION

Applicants believe that in light of the foregoing amendments and remarks, the claims are in condition for allowance, and accordingly, respectfully request withdrawal of the outstanding objections and rejections. An allowance is earnestly sought.

Respectfully submitted,
BAKER BOTTS, L.L.P.



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Peter J. Shen
PTO Reg. No. 52,217
Attorney for Applicants
BAKER BOTTS, L.L.P.
30 Rockefeller Plaza
New York, NY 10112
(212) 408-2500

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- La date de réception (sauf lorsque les lettres "NR" figurent dans la colonne de droite) par le Bureau international du ou des documents de priorité correspondant à la ou aux demandes énumérées ci-après est notifiée au déposant. Sauf indication contraire consistant en un astérisque figurant à côté d'une date de réception, ou les lettres "NR", dans la colonne de droite, le document de priorité en question a été présenté ou transmis au Bureau international d'une manière conforme à la règle 17.1.a) ou b).
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- Un **astérisque(*)** figurant à côté d'une date de réception dans la colonne de droite signale un document de priorité présenté ou transmis au Bureau international mais de manière non conforme à la règle 17.1.a) ou b). Dans ce cas, **l'attention du déposant est appelée** sur la règle 17.1.c) qui stipule qu'aucun office désigné ne peut décider de ne pas tenir compte de la revendication de priorité avant d'avoir donné au déposant la possibilité de remettre le document de priorité dans un délai raisonnable en l'espèce.
- Les **lettres "NR"** figurant dans la colonne de droite signalent un document de priorité que le Bureau international n'a pas reçu ou que le déposant n'a pas demandé à l'office récepteur de préparer et de transmettre au Bureau international, conformément à la règle 17.1.a) ou b), respectivement. Dans ce cas, **l'attention du déposant est appelée** sur la règle 17.1.c) qui stipule qu'aucun office désigné ne peut décider de ne pas tenir compte de la revendication de priorité avant d'avoir donné au déposant la possibilité de remettre le document de priorité dans un délai raisonnable en l'espèce.

<u>Date de priorité</u>	<u>Demande de priorité n°</u>	<u>Pays, office régional ou office récepteur selon le PCT</u>	<u>Date de réception du document de priorité</u>
28 juil 1999 (28.07.99)	99/09990	FR	17 octo 2000 (17.10.00)

Bureau international de l'OMPI
34, chemin des Colombettes
1211 Genève 20, Suisse

no de télécopieur (41-22) 740.14.35

Fonctionnaire autorisé:

Magda BOUACHA

no de téléphone (41-22) 338.83.38